

What is claimed is:

1. A tissue sealant composition, comprising a crosslinking agent, and a synthetic collagen or a synthetic gelatin, in a dry state,

wherein, in the dry state, the crosslinking agent does not react with the synthetic collagen or with the synthetic gelatin, and

wherein, upon contact with an environment comprising about a physiological pH, the crosslinking agent reacts with the synthetic collagen or the synthetic gelatin, thereby forming a tissue sealant composition

2. The composition of claim 1, wherein the synthetic collagen comprises a synthetic human collagen.

3. The composition of claim 1, wherein the synthetic collagen comprises type I collagen, type III collagen, or a combination of type I collagen and type III collagen.

4. The composition of claim 1, wherein the synthetic collagen comprises collagen of one type free of any other type of collagen.

5. The composition of claim 1, wherein the synthetic collagen comprises a recombinant collagen.

6. The composition of claim 1, wherein the synthetic gelatin comprises a human gelatin.

7. The composition of claim 1, wherein the synthetic gelatin comprises a recombinant gelatin.

8. The composition of claim 7, wherein the synthetic gelatin is derived from type I collagen, type III collagen, or a combination of type I collagen and type III collagen.

9. The composition of claim 1, wherein the crosslinking agent and the synthetic collagen or the synthetic gelatin comprise a mixture.

10. The composition of claim 1, wherein the crosslinker comprises an electrophilically activated (EA) poly(ethylene glycol) (PEG) or an EA PEG derivative.

11. The composition of claim 10, wherein the EA PEG derivative comprises a PEG-succinimidyl ester.

12. The composition of claim 11, wherein the PEG-succinimidyl ester is PEG-succinimidyl propionate, PEG-succinimidyl butanoate, or PEG-succinimidyl glutarate.

13. The composition of claim 10, wherein the EA PEG or EA PEG derivative comprises a branched EA PEG.

14. The composition of claim 13, wherein the branched EA PEG comprises a 4 arm EA PEG or an 8 arm EA PEG.

15. The composition of claim 12, wherein the crosslinker comprises 8 arm poly(ethylene glycol)-succinimidyl propionate.

16. The composition of claim 1, which further comprises a therapeutic agent.

17. The composition of claim 1, which further comprises a matrix scaffold.

18. The composition of claim 1, wherein the synthetic gelatin is derived from recombinant collagen of one type free of any other type of collagen.

19. The composition of claim 1, wherein the synthetic gelatin comprises homogeneous gelatin polypeptides.

20. The composition of claim 1, wherein the synthetic collagen comprises an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, or collagenous fragments thereof.

21. The composition of claim 1, wherein the synthetic gelatin comprises the amino acid sequence of SEQ ID NO:1.

22. The composition of claim 17, wherein the matrix scaffold comprises a synthetic gelatin.

23. The composition of claim 17, wherein the matrix scaffold comprises a human collagen.

24. The composition of claim 17, wherein the matrix scaffold comprises a synthetic collagen.

25. The composition of claim 24, wherein the synthetic collagen comprises type I collagen, type III collagen, or a combination of type I collagen and type III collagen.

26. The composition of claim 17, wherein the matrix scaffold comprises a synthetic gelatin derived from recombinant human type III collagen.

27. The composition of claim 1, wherein the crosslinking agent is a polymeric crosslinking agent.

28. The composition of claim 1, wherein the crosslinking agent is an electrophilic crosslinking agent.

29. The composition of claim 17, wherein the matrix scaffold comprises a reservoir.

30. The composition of claim 17, wherein the matrix scaffold comprises a reservoir containing a therapeutic agent.

31. The composition of claim 17, wherein the matrix scaffold comprises a reservoir containing an aqueous solution.

32. The composition of claim 31, wherein the aqueous solution comprises a basic salt solution.

33. The composition of claim 30, wherein the therapeutic agent comprises an antimicrobial agent, an antiviral agent, an antifungal agent, or a combination thereof.

34. The composition of claim 30, wherein the therapeutic agent comprises a cell or tissue growth factor.

35. The composition of claim 34, wherein the growth factor comprise connective tissue growth factor, fibroblast growth factor, or platelet derived growth factor, vascular endothelial growth factor, or a combination thereof.

36. The composition of claim 30, wherein the therapeutic agent comprises an agent that facilitates coagulation or reduces the rate of dissolution of a clot.

37. The composition of claim 1, wherein the tissue sealant composition further comprises a therapeutic agent.

38. The composition of claim 37, wherein the agent comprises an antimicrobial agent, an antiviral agent, an antifungal agent, or a combination thereof.

39. A method of producing a tissue sealant, the method comprising:  
drying a crosslinking agent, and a synthetic collagen or a synthetic gelatin,  
under conditions in which the crosslinking agent, when contacted with the

synthetic collagen or the synthetic gelatin under conditions other than an environment comprising about a physiological pH, does not react with the synthetic collagen or the synthetic gelatin, thereby producing tissue sealant components in a dry state; and

contacting tissue sealant components with an environment comprising about a physiological pH, whereby the crosslinker reacts with the synthetic collagen or with the synthetic gelatin, thereby producing a tissue sealant.

40. The method of claim 39, wherein the tissue sealant components are mixed, under conditions in which the crosslinking agent does not react with the synthetic collagen or the synthetic gelatin, prior to contacting the tissue sealant components with the environment comprising about a physiological pH.

41. A method of producing a tissue sealant, the method comprising:

mixing a and a synthetic collagen or a synthetic gelatin, under conditions in which the polymeric crosslinker does not react with the synthetic collagen or the synthetic gelatin, thereby producing a tissue sealant component mixture; and

drying the tissue sealant component mixture under said conditions, thereby producing a tissue sealant in a dry state.

42. The method of claim 41, wherein said mixing is performed in an aqueous acidic solution, thereby producing an aqueous acidic tissue sealant component mixture.

43. The method of claim 42, wherein said drying comprises freezing and lyophilizing the tissue sealant component mixture.

44. The method of claim 41, further comprising, prior to drying the tissue sealant component mixture, contacting the mixture with a matrix scaffold while maintaining said conditions, whereby, after drying the tissue sealant component admixture, a matrix scaffold comprising the tissue sealant in a dry state is produced.

45. The method of claim 44, further comprising, after drying the tissue sealant component admixture, applying the tissue sealant in a dry state to a matrix scaffold under conditions in which the crosslinker does not react with the tissue sealant.

46. The method of claim 41, which comprises:

admixing 8 arm poly(ethylene glycol)-succinimidyl propionate (PEG-SPA) and a gelatin derivative of recombinant human type I collagen in about a 1 mM hydrochloric acid solution, thereby producing an aqueous acidic tissue sealant component admixture; and

freezing and lyophilizing the aqueous acid tissue sealant component admixture, thereby producing a tissue sealant in a dry state.

47. The method of claim 46, further comprising, prior to freezing and lyophilizing the admixture, spraying the aqueous acidic tissue sealant component admixture onto a matrix scaffold comprising recombinant human type III collagen, thereby producing a coated matrix scaffold comprising the admixture,

whereby, after freezing and lyophilizing the aqueous acidic tissue sealant component admixture comprising the coated matrix scaffold, a matrix scaffold comprising the tissue sealant in a dry state is produced.

48. The method of claim 47, further comprising freezing the matrix scaffold prior to said spraying.

49. The method of claim 48, further comprising wetting the matrix scaffold with a basic salt solution prior to said freezing.

50. A method of sealing a wound, comprising contacting the wound with the tissue sealant composition of claim 1.

51. The method of claim 50, wherein the wound comprises a surgical incision.

52. The method of claim 50, wherein the surgical incision comprises an angioplasty.

53. The method of claim 50, wherein the wound comprises a laceration or a puncture.

54. The method of claim 50, wherein the tissue sealant composition further comprises a therapeutic agent.

55. A kit, comprising at least one crosslinking agent, and at least one of a synthetic collagen component or a synthetic gelatin component,

wherein, upon contact in a dry state, the polymeric crosslinking agent does not react with the synthetic collagen component or with the synthetic gelatin component, and

wherein, upon contact with an environment comprising about a physiological pH, the crosslinking agent reacts with the synthetic collagen component or the synthetic gelatin component to form a tissue sealant composition.

56. The kit of claim 55, wherein the crosslinking agent, and the synthetic collagen component or the synthetic gelatin component, comprise a mixture.